

# SEQUENCE LISTING

<110> Dale, Roderic M. K.  
Arrow, Amy  
Thompson, Terry

<120> Antisense Phosphodiesterase Inhibitors

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His Leu Ser Glu Met Ser Arg Ser Gly Asn Gln Val Ser Glu Tyr Ile  
35 40 45  
Ser Thr Thr Phe Leu Asp Lys Gln Asn Glu Val Glu Ile Pro Ser Pro  
50 55 60  
Thr Met Lys Glu Arg Glu Lys Gln Gln Ala Pro Arg Pro Arg Pro Ser  
65 70 75 80  
Gln Pro Pro Pro Pro Pro Val Pro His Leu Gln Pro Met Ser Gln Ile  
85 90 95  
Thr Gly Leu Lys Lys Leu Met His Ser Asn Ser Leu Asn Asn Ser Asn  
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Ile Pro Arg Phe Gly Val Lys Thr Asp Gln Glu Glu Leu Leu Ala Gln  
115 120 125  
Glu Leu Glu Asn Leu Asn Lys Trp Gly Leu Asn Ile Phe Cys Val Ser  
130 135 140  
Asp Tyr Ala Gly Gly Arg Ser Leu Thr Cys Ile Met Tyr Met Ile Phe  
145 150 155 160  
Gln Glu Arg Asp Leu Leu Lys Lys Phe Arg Ile Pro Val Asp Thr Met  
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Lys	Leu	Leu	Gln	Glu	Asp	Asn	Cys	Asp	Ile	Phe	Gln	Asn	Leu	Ser	Lys		
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Trp	Arg	Gln	Pro	Arg	Arg	Pro	Ile	Arg	Ile	Gln	Gln	Arg	Phe	Tyr	Ser	35	40	45	
Asp	Pro	Asp	Lys	Ser	Ala	Gly	Cys	Arg	Glu	Arg	Asp	Leu	Ser	Pro	Arg	50	55	60	
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Pro	Gln	Ser	Ser	Pro	Gly	Leu	Gly	Arg	Ile	Met	Gln	Ala	Pro	Val	Pro	100	105	110	
His	Ser	Gln	Arg	Arg	Glu	Ser	Phe	Leu	Tyr	Arg	Ser	Asp	Ser	Asp	Tyr	115	120	125	
Glu	Leu	Ser	Pro	Lys	Ala	Met	Ser	Arg	Asn	Ser	Ser	Val	Ala	Ser	Asp	130	135	140	
Leu	His	Gly	Glu	Asp	Met	Ile	Val	Thr	Pro	Phe	Ala	Gln	Val	Leu	Ala	145	150	155	160
Ser	Leu	Arg	Thr	Val	Arg	Ser	Asn	Val	Ala	Ala	Leu	Ala	Arg	Gln	Gln	165	170	175	
Cys	Leu	Gly	Ala	Ala	Lys	Gln	Gly	Pro	Val	Gly	Asn	Pro	Ser	Ser	Ser	180	185	190	
Asn	Gln	Leu	Pro	Pro	Ala	Glu	Asp	Thr	Gly	Gln	Lys	Leu	Ala	Leu	Glu	195	200	205	
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Thr	Arg	His	Ser	Val	Gly	Glu	Met	Ala	Ser	Asn	Lys	Phe	Lys	Arg	Ile	225	230	235	240
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Val	Glu	Leu	Pro	Lys	Val	Thr	Ala	Glu	Glu	Ala	Pro	Gln	Pro	Met	Ser	275	280	285	
Arg	Ile	Ser	Gly	Leu	His	Gly	Leu	Cys	His	Ser	Ala	Ser	Leu	Ser	Ser	290	295	300	
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Ala	Lys	Glu	Leu	Glu	Asp	Thr	Asn	Lys	Trp	Gly	Leu	Asp	Val	Phe	Lys	325	330	335	
Val	Ala	Asp	Val	Ser	Gly	Asn	Arg	Pro	Leu	Thr	Ala	Ile	Ile	Phe	Ser	340	345	350	
Ile	Phe	Gln	Glu	Arg	Asp	Leu	Leu	Lys	Thr	Phe	Gln	Ile	Pro	Ala	Asp	355	360	365	
Thr	Leu	Ala	Thr	Tyr	Leu	Leu	Met	Leu	Glu	Gly	His	Tyr	His	Ala	Asn	370	375	380	
Val	Ala	Tyr	His	Asn	Ser	Leu	His	Ala	Ala	Asp	Val	Ala	Gln	Ser	Thr	385	390	395	400
His	Val	Leu	Leu	Ala	Thr	Pro	Ala	Leu	Glu	Ala	Val	Phe	Thr	Asp	Leu	405	410	415	
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Ser Ala Lys Gln Arg Leu Ser Leu Arg Arg Met Val Ile Asp Met Val  
485 490 495  
Leu Ala Thr Asp Met Ser Lys His Met Asn Leu Leu Ala Asp Leu Lys  
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Thr Met Val Glu Thr Lys Lys Val Thr Ser Leu Gly Val Leu Leu Leu  
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Asp Asn Tyr Ser Asp Arg Ile Gln Val Leu Gln Asn Leu Val His Cys  
530 535 540  
Ala Asp Leu Ser Asn Pro Thr Lys Pro Leu Pro Leu Tyr Arg Gln Trp  
545 550 555 560  
Thr Asp Arg Ile Met Ala Glu Phe Phe Gln Gln Gly Asp Arg Glu Arg  
565 570 575  
Glu Ser Gly Leu Asp Ile Ser Pro Met Cys Asp Lys His Thr Ala Ser  
580 585 590  
Val Glu Lys Ser Gln Val Gly Phe Ile Asp Tyr Ile Ala His Pro Leu  
595 600 605  
Trp Glu Thr Trp Ala Asp Leu Val His Pro Asp Ala Gln Asp Leu Leu  
610 615 620  
Asp Thr Leu Glu Asp Asn Arg Glu Trp Tyr Gln Ser Lys Ile Pro Arg  
625 630 635 640  
Ser Pro Ser Asp Leu Thr Asn Pro Glu Arg Asp Gly Pro Asp Arg Phe  
645 650 655  
Gln Phe Glu Leu Thr Leu Glu Glu Ala Glu Glu Glu Asp Glu Glu Glu  
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Glu Glu Glu Gly Glu Glu Thr Ala Leu Ala Lys Glu Ala Leu Glu Leu  
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Gly Leu Asn Ile Phe	Asn Val Ala Gly Tyr Ser	His Asn Arg Pro Leu
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Thr Cys Ile Met Tyr	Ala Ile Phe Gln Glu Arg	Asp Leu Leu Lys Thr
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Phe Arg Ile Ser Ser	Asp Thr Phe Ile Thr Tyr	Met Met Thr Leu Glu
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225	230	235
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Ala Val Phe Thr Asp	Leu Glu Ile Leu Ala	Ala Ile Phe Ala Ala Ala
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Ile His Asp Val Asp	His Pro Gly Val Ser	Asn Gln Phe Leu Ile Asn
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Arg Asn Met Val His	Cys Ala Asp Leu Ser	Asn Pro Thr Lys Ser Leu
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Gln Gly Asp Lys Glu	Arg Glu Arg Gly Met	Glu Ile Ser Pro Met Cys
420	425	430
Asp Lys His Thr Ala	Ser Val Glu Lys Ser	Gln Val Gly Phe Ile Asp
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Tyr Ile Val His Pro	Leu Trp Glu Thr Trp	Ala Asp Leu Val Gln Pro
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Gln Ser Met Ile Pro	Gln Ser Pro Ser Pro	Pro Leu Asp Glu Gln Asn
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Arg Asp Cys Gln Gly	Leu Met Glu Lys Phe	Gln Phe Glu Leu Thr Leu
500	505	510
Asp Glu Glu Asp Ser	Glu Gly Pro Glu Lys	Glu Gly Glu Gly His Ser
515	520	525
Tyr Phe Ser Ser Thr	Lys Thr Leu Cys Val	Ile Asp Pro Glu Asn Arg
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Gln Lys Glu Lys Glu Lys Lys Lys Arg Pro Met Ser Gln Ile Ser Gly  
50 55 60  
Val Lys Lys Leu Met His Ser Ser Ser Leu Thr Asn Ser Ser Ile Pro  
65 70 75 80  
Arg Phe Gly Val Lys Thr Glu Gln Glu Asp Val Leu Ala Lys Glu Leu  
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Glu Asp Val Asn Lys Trp Gly Leu His Val Phe Arg Ile Ala Glu Leu  
100 105 110  
Ser Gly Asn Arg Pro Leu Thr Val Ile Met His Thr Ile Phe Gln Glu  
115 120 125  
Arg Asp Leu Leu Lys Thr Phe Lys Ile Pro Val Asp Thr Leu Ile Thr  
130 135 140  
Tyr Leu Met Thr Leu Glu Asp His Tyr His Ala Asp Val Ala Tyr His  
145 150 155 160  
Asn Asn Ile His Ala Ala Asp Val Val Gln Ser Thr His Val Leu Leu  
165 170 175  
Ser Thr Pro Ala Leu Glu Ala Val Phe Thr Asp Leu Glu Ile Leu Ala  
180 185 190  
Ala Ile Phe Ala Ser Ala Ile His Asp Val Asp His Pro Gly Val Ser  
195 200 205  
Asn Gln Phe Leu Ile Asn Thr Asn Ser Glu Leu Ala Leu Met Tyr Asn  
210 215 220  
Asp Ser Ser Val Leu Glu Asn His His Leu Ala Val Gly Phe Lys Leu  
225 230 235 240  
Leu Gln Glu Glu Asn Cys Asp Ile Phe Gln Asn Leu Thr Lys Lys Gln  
245 250 255  
Arg Gln Ser Leu Arg Lys Met Val Ile Asp Ile Val Leu Ala Thr Asp  
260 265 270  
Met Ser Lys His Met Asn Leu Leu Ala Asp Leu Lys Thr Met Val Glu  
275 280 285  
Thr Lys Lys Val Thr Ser Ser Gly Val Leu Leu Leu Asp Asn Tyr Ser  
290 295 300  
Asp Arg Ile Gln Val Leu Gln Asn Met Val His Cys Ala Asp Leu Ser  
305 310 315 320  
Asn Pro Thr Lys Pro Leu Gln Leu Tyr Arg Gln Trp Thr Asp Arg Ile  
325 330 335  
Met Glu Glu Phe Phe Arg Gln Gly Asp Arg Glu Arg Glu Arg Gly Met  
340 345 350  
Glu Ile Ser Pro Met Cys Asp Lys His Asn Ala Ser Val Glu Lys Ser  
355 360 365  
Gln Val Gly Phe Ile Asp Tyr Ile Val His Pro Leu Trp Glu Thr Trp  
370 375 380  
Ala Asp Leu Val His Pro Asp Ala Gln Asp Ile Leu Asp Thr Leu Glu  
385 390 395 400  
Asp Asn Arg Glu Trp Tyr Gln Ser Thr Ile Pro Gln Ser Pro Ser Pro  
405 410 415  
Ala Pro Asp Asp Pro Glu Glu Gly Arg Gln Gly Gln Thr Glu Lys Phe  
420 425 430  
Gln Phe Glu Leu Thr Leu Glu Glu Asp Gly Glu Ser Asp Thr Glu Lys  
435 440 445  
Asp Ser Gly Ser Gln Val Glu Glu Asp Thr Ser Cys Ser Asp Ser Lys  
450 455 460  
Thr Leu Arg Thr Gln Asp Ser Glu Ser Thr Glu Ile Pro Leu Asp Glu

465                      470                      475                      480  
 Gln Val Glu Glu Glu Ala Val Gly Glu Glu Glu Ser Gln Pro Glu  
                                  485                      490                      495  
 Ala Cys Val Ile Asp Asp Arg Ser Pro Asp Thr  
                                  500                      505

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 <212> PRT  
 <213> human

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 Asn Pro His Cys Pro Asn Pro Trp Leu Asn Glu Asp Leu Val Lys Ser  
                                  20                      25                      30  
 Leu Arg Glu Asn Leu Leu Gln His Glu Lys Ser Lys Thr Ala Arg Lys  
                                  35                      40                      45  
 Ser Val Ser Pro Lys Leu Ser Pro Val Ile Ser Pro Arg Asn Ser Pro  
                                  50                      55                      60  
 Arg Leu Leu Arg Arg Met Leu Leu Ser Ser Asn Ile Pro Lys Gln Arg  
 65                      70                      75                      80  
 Arg Phe Thr Val Ala His Thr Cys Phe Asp Val Asp Asn Gly Thr Ser  
                                  85                      90                      95  
 Ala Gly Arg Ser Pro Leu Asp Pro Met Thr Ser Pro Gly Ser Gly Leu  
                                  100                      105                      110  
 Ile Leu Gln Ala Asn Phe Val His Ser Gln Arg Arg Glu Ser Phe Leu  
                                  115                      120                      125  
 Tyr Arg Ser Asp Ser Asp Tyr Asp Leu Ser Pro Lys Ser Met Ser Arg  
                                  130                      135                      140  
 Asn Ser Ser Ile Ala Ser Asp Ile His Gly Asp Asp Leu Ile Val Thr  
 145                      150                      155                      160  
 Pro Phe Ala Gln Val Leu Ala Ser Leu Arg Thr Val Arg Asn Asn Phe  
                                  165                      170                      175  
 Ala Ala Leu Thr Asn Leu Gln Asp Arg Ala Pro Ser Lys Arg Ser Pro  
                                  180                      185                      190  
 Met Cys Asn Gln Pro Ser Ile Asn Lys Ala Thr Ile Thr Glu Glu Ala  
                                  195                      200                      205  
 Tyr Gln Lys Leu Ala Ser Glu Thr Leu Glu Glu Leu Asp Trp Cys Leu  
                                  210                      215                      220  
 Asp Gln Leu Glu Thr Leu Gln Thr Arg His Ser Val Ser Glu Met Ala  
 225                      230                      235                      240  
 Ser Asn Lys Phe Lys Arg Met Leu Asn Arg Glu Leu Thr His Leu Ser  
                                  245                      250                      255  
 Glu Met Ser Arg Ser Gly Asn Gln Val Ser Glu Phe Ile Ser Asn Thr  
                                  260                      265                      270  
 Phe Leu Asp Lys Gln His Glu Val Glu Ile Pro Ser Pro Thr Gln Lys  
                                  275                      280                      285  
 Glu Lys Glu Lys Lys Lys Arg Pro Met Ser Gln Ile Ser Gly Val Lys  
                                  290                      295                      300  
 Lys Leu Met His Ser Ser Ser Leu Thr Asn Ser Ser Ile Pro Arg Phe  
 305                      310                      315                      320  
 Gly Val Lys Thr Glu Gln Glu Asp Val Leu Ala Lys Glu Leu Glu Asp  
                                  325                      330                      335  
 Val Asn Lys Trp Gly Leu His Val Phe Arg Ile Ala Glu Leu Ser Gly  
                                  340                      345                      350  
 Asn Arg Pro Leu Thr Val Ile Met His Thr Ile Phe Gln Glu Arg Asp  
                                  355                      360                      365  
 Leu Leu Lys Thr Phe Lys Ile Pro Val Asp Thr Leu Ile Thr Tyr Leu  
                                  370                      375                      380

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Met Thr Leu Glu Asp His Tyr His Ala Asp Val Ala Tyr His Asn Asn  
 385 390 395 400  
 Ile His Ala Ala Asp Val Val Gln Ser Thr His Val Leu Leu Ser Thr  
 405 410 415  
 Pro Ala Leu Glu Ala Val Phe Thr Asp Leu Glu Ile Leu Ala Ala Ile  
 420 425 430  
 Phe Ala Ser Ala Ile His Asp Val Asp His Pro Gly Val Ser Asn Gln  
 435 440 445  
 Phe Leu Ile Asn Thr Asn Ser Glu Leu Ala Leu Met Tyr Asn Asp Ser  
 450 455 460  
 Ser Val Leu Glu Asn His His Leu Ala Val Gly Phe Lys Leu Leu Gln  
 465 470 475 480  
 Glu Glu Asn Cys Asp Ile Phe Gln Asn Leu Thr Lys Lys Gln Arg Gln  
 485 490 495  
 Ser Leu Arg Lys Met Val Ile Asp Ile Val Leu Ala Thr Asp Met Ser  
 500 505 510  
 Lys His Met Asn Leu Leu Ala Asp Leu Lys Thr Met Val Glu Thr Lys  
 515 520 525  
 Lys Val Thr Ser Ser Gly Val Leu Leu Leu Asp Asn Tyr Ser Asp Arg  
 530 535 540  
 Ile Gln Val Leu Gln Asn Met Val His Cys Ala Asp Leu Ser Asn Pro  
 545 550 555 560  
 Thr Lys Pro Leu Gln Leu Tyr Arg Gln Trp Thr Asp Arg Ile Met Glu  
 565 570 575  
 Glu Phe Phe Arg Gln Gly Asp Arg Glu Arg Glu Arg Gly Met Glu Ile  
 580 585 590  
 Ser Pro Met Cys Asp Lys His Asn Ala Ser Val Glu Lys Ser Gln Val  
 595 600 605  
 Gly Phe Ile Asp Tyr Ile Val His Pro Leu Trp Glu Thr Trp Ala Asp  
 610 615 620  
 Leu Val His Pro Asp Ala Gln Asp Ile Leu Asp Thr Leu Glu Asp Asn  
 625 630 635 640  
 Arg Glu Trp Tyr Gln Ser Thr Ile Pro Gln Ser Pro Ser Pro Ala Pro  
 645 650 655  
 Asp Asp Pro Glu Glu Gly Arg Gln Gly Gln Thr Glu Lys Phe Gln Phe  
 660 665 670  
 Glu Leu Thr Leu Glu Glu Asp Gly Glu Ser Asp Thr Glu Lys Asp Ser  
 675 680 685  
 Gly Ser Gln Val Glu Glu Asp Thr Ser Cys Ser Asp Ser Lys Thr Leu  
 690 695 700  
 Cys Thr Gln Asp Ser Glu Ser Thr Glu Ile Pro Leu Asp Glu Gln Val  
 705 710 715 720  
 Glu Glu Glu Ala Val Gly Glu Glu Glu Glu Ser Gln Pro Glu Ala Cys  
 725 730 735  
 Val Ile Asp Asp Arg Ser Pro Asp Thr  
 740 745

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<400> 51  
 Met Met His Val Asn Asn Phe Pro Phe Arg Arg His Ser Trp Ile Cys  
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 Phe Asp Val Asp Asn Gly Thr Ser Ala Gly Arg Ser Pro Leu Asp Pro  
 20 25 30  
 Met Thr Ser Pro Gly Ser Gly Leu Ile Leu Gln Ala Asn Phe Val His  
 35 40 45  
 Ser Gln Arg Arg Glu Ser Phe Leu Tyr Arg Ser Asp Ser Asp Tyr Asp



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50	55	60
Leu Ser Pro Lys Ser Met	Ser Arg Asn Ser Ser	Ile Ala Ser Asp Ile
65	70	75
His Gly Asp Asp Leu Ile Val Thr Pro Phe Ala Gln Val Leu Ala Ser		80
	85	90
Leu Arg Thr Val Arg Asn Asn Phe Ala Ala Leu Thr Asn Leu Gln Asp		95
	100	105
Arg Ala Pro Ser Lys Arg Ser Pro Met Cys Asn Gln Pro Ser Ile Asn		110
	115	120
Lys Ala Thr Ile Thr Glu Glu Ala Tyr Gln Lys Leu Ala Ser Glu Thr		125
	130	135
Leu Glu Glu Leu Asp Trp Cys Leu Asp Gln Leu Glu Thr Leu Gln Thr		140
145	150	155
Arg His Ser Val Ser Glu Met Ala Ser Asn Lys Phe Lys Arg Met Leu		160
	165	170
Asn Arg Glu Leu Thr His Leu Ser Glu Met Ser Arg Ser Gly Asn Gln		175
	180	185
Val Ser Glu Phe Ile Ser Asn Thr Phe Leu Asp Lys Gln His Glu Val		190
	195	200
Glu Ile Pro Ser Pro Thr Gln Lys Glu Lys Glu Lys Lys Arg Pro		205
	210	215
Met Ser Gln Ile Ser Gly Val Lys Lys Leu Met His Ser Ser Ser Leu		220
225	230	235
Thr Asn Ser Ser Ile Pro Arg Phe Gly Val Lys Thr Glu Gln Glu Asp		240
	245	250
Val Leu Ala Lys Glu Leu Glu Asp Val Asn Lys Trp Gly Leu His Val		255
	260	265
Phe Arg Ile Ala Glu Leu Ser Gly Asn Arg Pro Leu Thr Val Ile Met		270
	275	280
His Thr Ile Phe Gln Glu Arg Asp Leu Leu Lys Thr Phe Lys Ile Pro		285
	290	295
Val Asp Thr Leu Ile Thr Tyr Leu Met Thr Leu Glu Asp His Tyr His		300
305	310	315
Ala Asp Val Ala Tyr His Asn Asn Ile His Ala Ala Asp Val Val Gln		320
	325	330
Ser Thr His Val Leu Leu Ser Thr Pro Ala Leu Glu Ala Val Phe Thr		335
	340	345
Asp Leu Glu Ile Leu Ala Ala Ile Phe Ala Ser Ala Ile His Asp Val		350
	355	360
Asp His Pro Gly Val Ser Asn Gln Phe Leu Ile Asn Thr Asn Ser Glu		365
	370	375
Leu Ala Leu Met Tyr Asn Asp Ser Ser Val Leu Glu Asn His His Leu		380
385	390	395
Ala Val Gly Phe Lys Leu Leu Gln Glu Glu Asn Cys Asp Ile Phe Gln		400
	405	410
Asn Leu Thr Lys Lys Gln Arg Gln Ser Leu Arg Lys Met Val Ile Asp		415
	420	425
Ile Val Leu Ala Thr Asp Met Ser Lys His Met Asn Leu Leu Ala Asp		430
	435	440
Leu Lys Thr Met Val Glu Thr Lys Lys Val Thr Ser Ser Gly Val Leu		445
	450	455
Leu Leu Asp Asn Tyr Ser Asp Arg Ile Gln Val Leu Gln Asn Met Val		460
465	470	475
His Cys Ala Asp Leu Ser Asn Pro Thr Lys Pro Leu Gln Leu Tyr Arg		480
	485	490
Gln Trp Thr Asp Arg Ile Met Glu Glu Phe Phe Arg Gln Gly Asp Arg		495
	500	505
Glu Arg Glu Arg Gly Met Glu Ile Ser Pro Met Cys Asp Lys His Asn		510
	515	520
Ala Ser Val Glu Lys Ser Gln Val Gly Phe Ile Asp Tyr Ile Val His		525

530					535					540				
Pro	Leu	Trp	Glu	Thr	Trp	Ala	Asp	Leu	Val	His	Pro	Asp	Ala	Gln
545					550					555				560
Ile	Leu	Asp	Thr	Leu	Glu	Asp	Asn	Arg	Glu	Trp	Tyr	Gln	Ser	Thr
				565					570					575
Pro	Gln	Ser	Pro	Ser	Pro	Ala	Pro	Asp	Asp	Pro	Glu	Glu	Gly	Arg
			580					585					590	Gln
Gly	Gln	Thr	Glu	Lys	Phe	Gln	Phe	Glu	Leu	Thr	Leu	Glu	Glu	Asp
		595					600					605		Gly
Glu	Ser	Asp	Thr	Glu	Lys	Asp	Ser	Gly	Ser	Gln	Val	Glu	Glu	Asp
	610					615				620				Thr
Ser	Cys	Ser	Asp	Ser	Lys	Thr	Leu	Cys	Thr	Gln	Asp	Ser	Glu	Ser
625					630					635				640
Glu	Ile	Pro	Leu	Asp	Glu	Gln	Val	Glu	Glu	Glu	Ala	Val	Gly	Glu
				645				650					655	Glu
Glu	Glu	Ser	Gln	Pro	Glu	Ala	Cys	Val	Ile	Asp	Asp	Arg	Ser	Pro
			660					665					670	Asp
Thr														

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